

STIC-ILL

From: Marx, Irene
Sent: Monday, June 14, 1999 1:46 PM
To: STIC-ILL
Subject: 09/083198

Please send to Irene Marx, Art Unit 1651; CM1, 10E05, 308-2922

Metabolic inhibitors, elicitors, and precursors as tools for probing yield limitation in taxane production by *Taxus chinensis* cell cultures

AU Srinivasan, V.; Ciddi, V.; ***Bringi, V.*** ; Shuler, M. L.
CS School of Chemical Engineering, Cornell University, Ithaca, NY, 14853, USA
SO Biotechnol. Prog. (1996), 12(4), 457-465

Large scale production of secondary metabolites using plant cell cultures:

Opportunities, realities and challenges.

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SO Abstracts of Papers American Chemical Society, (1997) Vol. 213, No. 1-3,
pp. AGFD 54.
Meeting Info.: 213th National Meeting of the American Chemical Society San
Francisco, California, USA April 13-17, 1997

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Production of ***taxol*** by cell culture of *Taxus*. For development of
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AU Hara, Yasuhiro; Yukimune, Yukihito
CS Mitsui Petrochem. Ind., Ltd., Yamaguchi, 740, Japan
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CODEN: FARUAW; ISSN: 0014-8601
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is metal toxicities. Evidence has emerged that non-
-ay significantly alter the overall oxidative status of
- due to a given oxidant is inversely related to the
- stress by generating oxidant signals to mobilize a
- vity of those enzymes have an effect on cellular
- und retained in wine have been found *in vitro*, to
- late nitric oxidation production and promote vaso-
- important to foods, plants and humans. Nutrients that
- as valuable not only in combating the deteriorative
- signaling that is an integral part of the response.

ATECHIN IN RATS. M. K. Piskula, J. Terao, - 305, Japan

the defence system of organism against oxidative
- wing positive influence of dietary flavonoids on
- the antioxidant activity of flavonoids in different
- ts after ingestion and absorption. Looking for an
- of (-)-epicatechin (EC), a commonly consumed
- isma level of metabolites was measured. 1h after
- C-glucuronide (11 μM), EC-glucuronide-sulfate
- while the concentration of the first two started to
- 3 hours, the third one had its maximum 1h later
- ab. 50% of all EC metabolites. Studies on the site
- stated EC is glucuronidation, occurring already on
- portal vein exclusively in a conjugated form and

HAMSTER MODEL. Dietrich Rein¹, Wallace H.
and Sci. & Tech. University of California, Davis,
Albany, CA 94710

ind seed oils moderate the development of
- sent in these foods. The aim of this study was to
- o test the effects of food components on the
- lipid deposition was investigated in hamsters fed
- increment of 3 IU or 30 IU vitamin E. After 30
- ten groups, and the high density lipoprotein
- ; atherogenic. Atherosclerosis was measured by
- new photomicroscopy scanning technique. The
- than in the 3 IU vitamin E group ($p < 0.03$). This
- 1-6 and n-3 fatty acids together with cholesterol
- to vitamin E with respect to the development of
- effects of individual food components *in vivo*.

TIVITIES OF α-TOCOPHEROL AND ITS
- rao². ¹Noda Institute for Scientific Research,
- ch Institute, Tsukuba, Ibaraki 305, Japan.
- it and to suppress the oxidative hemolysis of
- yl derivative of α-tocopherol (phosphatidyl-
- α-tocopherol, PCh, and 2,2,5,7,8-
- ian erythrocytes, it was found that the

antihemolytic activity was significantly enhanced by introducing phospholipid moiety into chromanol. PCh was incorporated into erythrocyte membrane and acted as an effective protector against oxidative hemolysis and membrane lipid peroxidation. The erythrocyte into which PCh was incorporated also has an inhibitory effect against the accumulation of cholesterol ester hydroperoxides in plasma. The relationship between structure of α-tocopherol derivatives and their antioxidant and antihemolytic activities will be discussed.

052. INTERACTIONS OF TOCOPHEROL AND FATTY ACIDS WITH MODEL - PHOSPHOLIPID MEMBRANES: IMPLICATIONS FOR ANTIOXIDANT ACTIVITY OF - VITAMIN E. D.F. Church, * T.R. Dugas, # J.D. Blazier, # G.M. Pineda, # *Radical Technologies, - Baton Rouge, LA 70810 and #Department of Chemistry, Louisiana State University, Baton Rouge, - LA 70803.

Kinetic studies show that α-tocopherol inhibits lipid peroxidation in unilamellar liposomes too slowly to act as an effective antioxidant at physiologically relevant concentrations. Antioxidant effectiveness is restored when free oleic acid is also incorporated into the model system. ESR spin-label measurements of the inclusion volumes of liposomes with added tocopherol and/or oleic acid suggest that neither of these, alone or together, substantially affect liposome structure. Both spin-label and differential scanning calorimetry studies show that tocopherol significantly increases membrane order and decreases fluidity, while the inclusion of oleic acid reverses these changes. Thus, physico-chemical interactions between tocopherol, free fatty acids and membrane phospholipids appear to control the inhibition of lipid peroxidation in membranes by tocopherol.

053. ANTIOXIDANT EVALUATION OF PHYTOCHEMICALS IN BIOLOGICAL SYSTEMS. E.N. - Frankel, Department of Food Science & Technology, University of California, Davis, California 95616

The true impact of biological oxidation is very controversial because of the questionable methodology used to measure lipid oxidation. Several non-specific assays have been introduced recently to test the "antioxidant capacity" of biological tissues and fluids, using artificial radicals as probes. These non-specific methods do not provide any information on what lipid or protein target is protected and may be confounded by many factors in complex biological systems including effects that may not be derived from lipid oxidation. To learn about the real effects of antioxidants, it is important to obtain specific chemical information about what products of lipid oxidation are inhibited. Several specific assays are needed to elucidate how lipid oxidation products act in the complex multi-step mechanism of lipid oxidative deterioration and damage in biological tissues. The methodology to evaluate natural antioxidants must be carefully interpreted depending on the system and the method used to determine lipid oxidation.

054. LARGE SCALE PRODUCTION OF SECONDARY METABOLITES USING PLANT CELL CULTURES: - OPPORTUNITIES, REALITIES AND CHALLENGES - K. Venkat, V. Bringi, P. Kadkade, and C. Prince, Phyton, Inc., Ithaca, NY 14850

The plant kingdom has historically been a major source of valuable medicinal compounds and healing agents. Unfortunately these compounds often occur in low yields in nature; further they require complex isolation and purification procedures. Plant cell culture technology offers a potential means to address these problems. Although elements of this technology have been around for many years, its widespread commercial use have not been possible due to a number of factors. Recent developments have brought this technology much closer to commercial application to large scale manufacturing of therapeutic and other valuable products.

Phyton has invested more than 150 man-years of effort to address the commercial issues of plant cell culture technology. Under a long-term collaborative relationship with Bristol-Myers Squibb (BMS) Company, Phyton is engaged in the development and commercialization of a plant cell culture process for the production of paclitaxel (the active ingredient of Taxol®; Taxol is the registered trademark of BMS). Through its wholly-owned subsidiary, Phyton Gesellschaft für Biotechnik mbH, Phyton operates the world's largest dedicated plant cell culture facility in Ahrensburg, Germany. It has a bioreactor capacity of up to 75,000 liters in size.

Several key issues relating to the development and practice of commercial plant cell culture processes for Taxol® and other high value compounds will be discussed.